REMARKS

This is in response to the Official Action mailed August 20, 2007, in which claims 7-11 stand rejected as obvious over Winther et al. ("Winther") in view of Fechteler et al. ("Fechteler"). Reconsideration is respectfully requested. The Examiner alleges that the claimed invention would have been obvious from Winther and Fechteler. Applicant respectfully disagrees.

The cited references teach, at most, the individual steps a) and b) of the claimed process, but clearly do not suggest the process as a whole.

Specifically, Winther discloses identification of nucleotides, proteins, compounds and/or pharmaceutical agents that either inhibit or enhance the activity of fatty acid delta-6-desaturase (also known as FADS2) involved in lipid metabolism and/or effectively regulate the level of expression of the delta-6-desaturase genes. See page 1, paragraph entitled "Field of invention."

In detail, Winther teaches the isolation, cloning, and identification of the control region (*i.e.* promoter and other regulatory elements) of both a human and a rat fatty acid desaturase gene, and the use of the desaturase gene control region in drug screening methods to identify test components which can effectively modulate desaturase gene expression. See page 12, 4th paragraph. The isolated nucleic acid sequences encoding desaturase enzymes have utility in constructing *in vivo* and/or *in vitro* experimental models for identifying components which modulate mammalian fatty acid desaturase activity and/or the level and regulation of desaturase gene expression. Additionally, the modulation or regulation of fatty acid desaturase enzyme activity or gene expression by various test components identified can be used to reduce disease processes or symptoms. See page 14, 1st paragraph.

As disclosed in Winther, test components having the potential to modulate desaturase activity can be identified by contacting a transformed host cell with the test component for a fixed period of time, and determining the level of lipid metabolite (*e.g.*, the level of product produced from a substrate) within the treated cells. See page 37, 1st paragraph. In contrast to the present application, Winther thus teaches an experimental procedure comprising one-step only, namely the evaluation of desaturase enzymatic activity in the presence of different test components. Nothing in Winther discloses or suggests subjecting the identified modulators of fatty acid metabolism to a further screening step, as required by the present claims.

Moreover, Winther does not teach that FADS2 may be part of an intracellular protein complex. In fact, Winther is completely silent on intracellular molecules being capable of interacting with FADS2. Additionally, Winther does not disclose that gamma secretase is part of a protein complex in which FADS2 is involved. This is not surprising because Winther focuses on desaturases and fatty acid metabolism, while gamma secretase is a protease.

It is therefore clear that Winther does not provide a structural or functional link between FADS2 and gamma secretase. Furthermore, as discussed above, Winther discloses only a one-step screening assay and gives no hint that a two-step screening assay may be beneficial for identifying gamma secretase modulators as claimed.

On the other hand, Fechteler teaches a process for finding substances capable of specifically inhibiting membrane-based proteases, and a high throughput sampling test for finding substances which are capable of specifically inhibiting gamma secretase and presenilinase. See page 4, lines 6-10.

The Fechteler process can be characterized as follows: (1) cells are cultivated which have said protease activity endogenously or exogenously and express a membrane-associated recombinant fusion protein which comprises the substrate of said protease with the specific cleavage site for said protease and a reporter, (2) these cells are incubated with a test substance, (3) the quantity of reporter cleaved is measured, and (4) the value obtained is compared with the value obtained in the absence of the test substance. See page 6, lines 7-20. As the method taught in Winther, Fechteler also teaches only a one-step procedure, namely the determination of gamma secretase activity in presence of a given substance. Fechteler does not disclose or suggest performing a two-step screening process, as required by the present claims.

Additionally, Fechteler is silent as to intracellular interaction partners of gamma secretase. Moreover, Fechteler does not disclose that gamma secretase is part of a protein complex including FADS2. This is not surprising, because Fechteler focuses on a protease, namely gamma secretase, while FADS2 is a molecule involved in fatty acid metabolism.

Accordingly, neither Winther nor Fechteler teaches or suggests that gamma secretase activity might be modulated by FADS2-interacting molecules, or that gamma secretase either directly or indirectly interacts with FADS2 in cells. Therefore, there is no suggestion or motivation to combine the teaching of Winther and Fechteler. Rather, because Winther and

Fechteler belong to two different biological fields, namely fatty acid metabolism and protease actions, one skilled person in the art is lead away from combining these references.

The Examiner contends that alleged "general knowledge" in the art recognized that gamma secretase is a holoenzyme comprising Presenilin, Nicastrin and Pen2 subunits, and each of which is associated with FADS2. As discussed above, neither Winther nor Fechteler discloses such an association and Applicant disagrees with the Examiner's assumption. The undersigned has been authorized to represent that, insofar as known, Applicant was the first to experimentally determine the association between gamma secretase and FADS2, as disclosed in the present application. See Specification at page 3, 3rd full paragraph. The interaction between FADS2 and members of the gamma secretase holoenzyme was not general knowledge in the art at the time the invention was made, and it is respectfully requested that the Examiner points to specific evidence in the record to support his finding.

In the absence of such evidence, the only rationale supporting the rejection cannot stand on the present record, since no other reason for combining Winther with Fechteler has been offered. As explained in M.P.E.P. § 2142 (8th Ed., revision 6), a post-*KSR* analysis still requires clear articulation why the claimed invention would have been obvious. It is still important "to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way that the claimed invention does." M.P.E.P. § 2143, citing *KSR International Co. v. Teleflex Inc.*, 82 USPQ 2d 1385, 1396 (2007). Applicant maintains that the obviousness rejection is factually unsupported by the record, and that only hindsight permits combination of the references as proposed.

CONCLUSION

For at least the above reasons, Applicant respectfully requests withdrawal of the rejections and allowance of the claims.

Accompanying this response is a petition for a one-month extension of time to and including December 20, 2007, to respond to the Office Action mailed August 20, 2007, and a Request for Continued Examination with the required fee authorization. If any additional fee is due, please charge our Deposit Account No. 03-2775, under Order No. 14129-00001-US from which the undersigned is authorized to draw.

Respectfully submitted,

By _____

Hui-Ju Wu, Ph.D.
Registration No.: 57,209
CONNOLLY BOVE LODGE & HUTZ LLP
1007 North Orange Street
P.O. Box 2207
Wilmington, Delaware 19899
(302) 658-9141
(302) 658-5614 (Fax)
Agent for Applicant

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